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* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 4 OCT 03 MATHDI removed from STN
NEWS 5 OCT 04 CA/Caplus-Canadian Intellectual Property Office (CIPO) added
to core patent offices
NEWS 6 OCT 13 New CAS Information Use Policies Effective October 17, 2005
NEWS 7 OCT 17 STN(R) AnaVist(TM), Version 1.01, allows the export/download
of Caplus documents for use in third-party analysis and
visualization tools
NEWS 8 OCT 27 Free KWIC format extended in full-text databases
NEWS 9 OCT 27 DIOGENES content streamlined
NEWS 10 OCT 27 EPFULL enhanced with additional content
NEWS 11 NOV 14 CA/Caplus - Expanded coverage of German academic research
NEWS 12 NOV 30 REGISTRY/ZREGISTRY on STN(R) enhanced with experimental
spectral property data
NEWS 13 DEC 05 CASREACT(R) - Over 10 million reactions available

NEWS EXPRESS DECEMBER 02 CURRENT VERSION FOR WINDOWS IS V8.01,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 02 DECEMBER 2005.
V8.0 USERS CAN OBTAIN THE UPGRADE TO V8.01 AT
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NEWS INTER General Internet Information
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of commercial gateways or other similar uses is prohibited and may
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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 09:22:46 ON 14 DEC 2005

=> file reg

COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 09:22:55 ON 14 DEC 2005

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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 13 DEC 2005 HIGHEST RN 869843-02-7
DICTIONARY FILE UPDATES: 13 DEC 2005 HIGHEST RN 869843-02-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> E "SULINDAC"/CN 25

E1	1	SULIKOL K/CN
E2	1	SULIN/CN
E3	1 -->	SULINDAC/CN
E4	1	SULINDAC B Ω -N-METHYL-L-ARGININE SALT/CN
E5	1	SULINDAC B Ω -N-NITRO-L-ARGININE METHYL ESTER SALT/CN
E6	1	SULINDAC B Ω -N-NITRO-L-ARGININE SALT/CN
E7	1	SULINDAC ETHYL ESTER/CN
E8	1	SULINDAC SODIUM/CN
E9	1	SULINDAC SULFIDE/CN
E10	1	SULINDAC SULFONE/CN
E11	1	SULINDAC SULFOXIDE/CN
E12	1	SULINDAC-QUINOLINE/CN
E13	1	SULINEX/CN
E14	1	SULINOL/CN
E15	1	SULIODOVIZOL/CN
E16	1	SULISATIN/CN
E17	1	SULISATIN DISODIUM SALT/CN
E18	1	SULISATIN SODIUM/CN
E19	1	SULISATINE SODIUM/CN
E20	1	SULISOBENZONE/CN
E21	1	SULJEX/CN
E22	1	SULKA/CN
E23	1	SULKA K BOLUSES/CN
E24	1	SULKA N/CN
E25	1	SULKOR/CN

=> S E3

L1 1 SULINDAC/CN

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
5.03	5.24

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 09:23:34 ON 14 DEC 2005
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FILE COVERS 1907 - 14 Dec 2005 VOL 143 ISS 25
FILE LAST UPDATED: 13 Dec 2005 (20051213/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

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=> s l1

L2 1426 L1

=> s gastrointestinal or esophag? or gastic? or intestin? or colorect?

2 GASTROINTESTINAL

15568 ESOPHAG?

4 GASTIC?

239459 INTESTIN?

18675 COLORECT?

L3 254068 GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLORECT?
T?

=> s cancer? or tumor? or neoplas? or polyp?

277857 CANCER?

411659 TUMOR?

431921 NEOPLAS?

438716 POLYP?

L4 1099978 CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?

=> s l4 and l3

L5 65506 L4 AND L3

=> s l5 and l2

L6 234 L5 AND L2

=> s oral?

L7 243958 ORAL?

=> s l7 and l6

L8 30 L7 AND L6

=> s l2 (1) l4

L9 186 L2 (L) L4

=> s l9 and l3

L10 121 L9 AND L3

=> s 110 and 17

L11 14 L10 AND L7

=> s 114 not py>2002

L14 NOT FOUND

The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s 111 not py>2002

3346380 PY>2002

L12 9 L11 NOT PY>2002

=> d ibib 1-4

L12 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:723268 CAPLUS

DOCUMENT NUMBER: 138:13001

TITLE: A mouse model of human oral-esophageal cancer

AUTHOR(S): Opitz, Oliver G.; Harada, Hideki; Suliman, Yasir; Rhoades, Ben; Sharpless, Norman E.; Kent, Ralph; Kopelovich, Levy; Nakagawa, Hiroshi; Rustgi, Anil K.

CORPORATE SOURCE: Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA, 19104-2144, USA

SOURCE: Journal of Clinical Investigation (2002), 110(6), 761-769

CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:259707 CAPLUS

DOCUMENT NUMBER: 136:379639

TITLE: Primary chemoprevention of familial adenomatous polyposis with sulindac

AUTHOR(S): Giardiello, Francis M.; Yang, Vincent W.; Hyland, Linda M.; Krush, Anne J.; Petersen, Gloria M.; Trimbath, Jill D.; Piantadosi, Steven; Garrett, Elizabeth; Geiman, Deborah E.; Hubbard, Walter; Offerhaus, Johan A.; Hamilton, Stanley R.

CORPORATE SOURCE: Dep. Med., Johns Hopkins Univ. Sch. Med., Baltimore, MD, USA

SOURCE: New England Journal of Medicine (2002), 346(14), 1054-1059

CODEN: NEJMAG; ISSN: 0028-4793

PUBLISHER: Massachusetts Medical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:564792 CAPLUS

DOCUMENT NUMBER: 135:127230

TITLE: Method for inhibiting a tumor

INVENTOR(S): Nair, Muraleedharan G.; Bourquin, Leslie D.; Seeram, Navindra P.; Kang, Soo-Young

PATENT ASSIGNEE(S): Michigan State University, USA

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054516	A1	20010802	WO 2001-US1196	20010112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2398389	AA	20010802	CA 2001-2398389	20010112
PRIORITY APPLN. INFO.:			US 2000-494077	A 20000128
			WO 2001-US1196	W 20010112
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L12 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:476884 CAPLUS
DOCUMENT NUMBER: 135:282815
TITLE: Sulindac in familial adenomatous polyposis: Evaluation by nuclear morphometry
AUTHOR(S): Fernandez-Lopez, F.; Conde-Freire, R.; Cadarso-Suarez, C.; Garcia-Iglesias, J.; Puente-Dominguez, J. L.; Potel-Lesquereux, J.
CORPORATE SOURCE: General Surgery Department, Hospital Clinico Universitario, Santiago de Compostela, Spain
SOURCE: European Journal of Surgery (2001), 167(5), 375-381
CODEN: EUJSEH; ISSN: 1102-4151
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib 5-9

L12 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:260877 CAPLUS
DOCUMENT NUMBER: 133:217169
TITLE: Sulindac and acetylsalicylic acid (ASA) - clinical relevance in familial adenomatous polyposis
AUTHOR(S): Winde, G.
CORPORATE SOURCE: Klinik und Poliklinik fur Allgemeine Chirurgie der WWU, Munster, D-48129, Germany
SOURCE: Falk Symposium (1999), 109(Colorectal Cancer), 235-255
CODEN: FASYDI; ISSN: 0161-5580
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:147314 CAPLUS
DOCUMENT NUMBER: 132:273995
TITLE: Inhibition of rat colon tumors by sulindac and sulindac sulfone is independent of K-ras (codon 12)

AUTHOR(S): mutation
 De Jong, Tanya A.; Skinner, Stewart A.;
 Malcontenti-Wilson, Cathy; Vogliagis, Daphne; Bailey,
 Michael; Van Driel, Ian R.; O'Brien, Paul E.
 CORPORATE SOURCE: Department of Surgery, Monash University Medical
 School, Melbourne, 3181, Australia
 SOURCE: American Journal of Physiology (2000), 278(2, Pt. 1),
 G266-G272
 CODEN: AJPHAP; ISSN: 0002-9513
 PUBLISHER: American Physiological Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 2000:18902 CAPLUS
 DOCUMENT NUMBER: 132:44655
 TITLE: Rectal epithelial apoptosis in familial adenomatous
 polyposis patients treated with sulindac
 AUTHOR(S): Keller, J. J.; Offerhaus, G. J. A.; Polak, M.;
 Goodman, S. N.; Zahurak, M. L.; Hyland, L. M.;
 Hamilton, S. R.; Giardiello, F. M.
 CORPORATE SOURCE: Department of Medicine, The Johns Hopkins University
 School of Medicine, Baltimore, MD, 21205, USA
 SOURCE: Gut (1999), 45(6), 822-828
 CODEN: GUTTAK; ISSN: 0017-5749
 PUBLISHER: BMJ Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1996:277228 CAPLUS
 DOCUMENT NUMBER: 124:331957
 TITLE: Sulindac induced regression of colorectal
 adenomas in familial adenomatous polyposis: Evaluation
 of predictive factors
 AUTHOR(S): Giardiello, F. M.; Offerhaus, J. A.; Tersmette, A. C.;
 Hyland, L. M.; Krush, A. J.; Brensinger, J. D.;
 Booker, S. V.; Hamilton, S. R.
 CORPORATE SOURCE: School Medicine, Johns Hopkins University, Baltimore,
 MD, 21287, USA
 SOURCE: Gut (1996), 38(4), 578-581
 CODEN: GUTTAK; ISSN: 0017-5749
 PUBLISHER: BMJ Publishing Group
 DOCUMENT TYPE: Journal
 LANGUAGE: English

L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1991:529697 CAPLUS
 DOCUMENT NUMBER: 115:129697
 TITLE: Lung tumorigenicity of NNK given orally to
 A/J mice: its application to chemopreventive efficacy
 studies
 AUTHOR(S): Castonguay, Andre; Pepin, Pierrot; Stoner, Gary D.
 CORPORATE SOURCE: Sch. Pharm., Laval Univ., Quebec, QC, G1K 7P4, Can.
 SOURCE: Experimental Lung Research (1991), 17(2), 485-99
 CODEN: EXLRDA; ISSN: 0190-2148
 DOCUMENT TYPE: Journal
 LANGUAGE: English

L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

AB The ability of five chemopreventive agents to inhibit 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)-induced lung tumors in A/J mice was determined. The carcinogen was administered in the drinking water during 7 wk (at doses of 9.2 to 3.1 mg/mouse). Three chemopreventive agents: (dose, g/kg diet) ellagic acid (4.0), 2(3)-BHA (5.0), and sulindac (0.13) inhibited the multiplicity of lung adenomas by 52, 88, and 52%, resp., when compared to NNK controls. β -Carotene + retinol (2.14 + 0.009), in combination, and selenium (0.0022) were ineffective. NNK was absorbed more rapidly from the duodenum than from the stomach and was metabolized in both tissues. The activation of NNK by α -carbon hydroxylation and its deactivation by pyridine N-oxidation was more extensive in the duodenum than in the stomach. Carbonyl reduction of NNK was 10 times higher in the duodenum. Liver microsomes were more active than lung microsomes in the α -carbon hydroxylation of NNK, suggesting that some liver isoenzymes of cytochrome P 450 have a high affinity for NNK. Pyridine N-oxidation was five times more extensive in lung microsomes than in liver microsomes. Collectively, these results demonstrate that NNK given orally to A/J mice provides a suitable model from which to assess the relative activity and mechanisms of action of chemopreventive agents in pulmonary carcinogenesis.

=> d kwic 9

L12 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

TI Lung tumorigenicity of NNK given orally to A/J mice: its application to chemopreventive efficacy studies

AB N-oxidation was five times more extensive in lung microsomes than in liver microsomes. Collectively, these results demonstrate that NNK given orally to A/J mice provides a suitable model from which to assess the relative activity and mechanisms of action of chemopreventive. . . .

IT Intestine, metabolism

(duodenum, ((methylnitrosamino)(pyridyl)butanone metabolism by, chemopreventive agents against lung neoplasm effect on)

IT 68-26-8, Retinol 476-66-4, Ellagic acid 7235-40-7, β -Carotene 14124-67-5, Selenite 25013-16-5 38194-50-2, Sulindac

RL: BIOL (Biological study)

((methylnitrosamino)(pyridyl)butanone-induced lung neoplasm response to)

=> d ibib abs keic 8

'KEIC' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS ----- GI and AB
ALL ----- BIB, AB, IND, RE
APPS ----- AI, PRAI
BIB ----- AN, plus Bibliographic Data and PI table (default)
CAN ----- List of CA abstract numbers without answer numbers
CBIB ----- AN, plus Compressed Bibliographic Data
DALL ----- ALL, delimited (end of each field identified)
DMAX ----- MAX, delimited for post-processing
FAM ----- AN, PI and PRAI in table, plus Patent Family data
FBIB ----- AN, BIB, plus Patent FAM
IND ----- Indexing data
IPC ----- International Patent Classifications
MAX ----- ALL, plus Patent FAM, RE
PATS ----- PI, SO
SAM ----- CC, SX, TI, ST, IT
SCAN ----- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,

e.g., D SCAN or DISPLAY SCAN)

STD ----- BIB, IPC, and NCL

IABS ----- ABS, indented with text labels

IALL ----- ALL, indented with text labels

IBIB ----- BIB, indented with text labels

IMAX ----- MAX, indented with text labels

ISTD ----- STD, indented with text labels

OBIB ----- AN, plus Bibliographic Data (original)

OIBIB ----- OBIB, indented with text labels

SBIB ----- BIB, no citations

SIBIB ----- IBIB, no citations

HIT ----- Fields containing hit terms

HITIND ----- IC, ICA, ICI, NCL, CC and index field (ST and IT)
containing hit terms

HITRN ----- HIT RN and its text modification

HITSTR ----- HIT RN, its text modification, its CA index name, and
its structure diagram

HITSEQ ----- HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields

FHITSTR ----- First HIT RN, its text modification, its CA index name, and
its structure diagram

FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields

KWIC ----- Hit term plus 20 words on either side

OCC ----- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR, FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC to view a specified Accession Number.

ENTER DISPLAY FORMAT (BIB):end

=> d ibib abs kwic 8

L12 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:277228 CAPLUS

DOCUMENT NUMBER: 124:331957

TITLE: Sulindac induced regression of colorectal
adenomas in familial adenomatous polyposis: Evaluation
of predictive factors

AUTHOR(S): Giardiello, F. M.; Offerhaus, J. A.; Tersmette, A. C.;
Hyland, L. M.; Krush, A. J.; Brensinger, J. D.;
Booker, S. V.; Hamilton, S. R.

CORPORATE SOURCE: School Medicine, Johns Hopkins University, Baltimore,
MD, 21287, USA

SOURCE: Gut (1996), 38(4), 578-581
CODEN: GUTTAK; ISSN: 0017-5749

PUBLISHER: BMJ Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background-Sulindac, a non-steroidal anti-inflammatory drug, causes
regression of colorectal adenomas in patients with familial
adenomatous polyposis (FAP) but the response is variable. Specific clin.
factors predictive of sulindac induced regression have not been studied.
Methods-22 patients with FAP were given sulindac 150 mg orally

twice a day. Polyp number and size were determined before treatment and at three

months. The relation of nine clin. factors to polyp regression (per cent of baseline polyp number after treatment) was evaluated by univariate and multivariate anal. Results-After three months of sulindac, polyp number had decreased to 45 per cent of baseline and polyp size to 50 per cent of baseline ($p < 0.001$ and $p < 0.01$, resp.). Univariate anal. showed greater polyp regression in older patients ($p = 0.004$), those with previous colectomy and ileorectal anastomosis ($p = 0.001$), and patients without identifiable mutation of the APC gene responsible for FAP ($p = 0.05$). With multivariate regression anal., response to sulindac treatment was associated with previous subtotal colectomy. Conclusions-Sulindac treatment seems effective in producing regression of colorectal adenomas of FAP patients with previous subtotal colectomy regardless of baseline polyp number and size. Changed sulindac metabolism, reduced area of the target mucosa, or changed epithelial characteristics after ileorectal anastomosis may explain these findings.

TI Sulindac induced regression of colorectal adenomas in familial adenomatous polyposis: Evaluation of predictive factors

AB Background-Sulindac, a non-steroidal anti-inflammatory drug, causes regression of colorectal adenomas in patients with familial adenomatous polyposis (FAP) but the response is variable. Specific clin. factors predictive of sulindac induced regression have not been studied. Methods-22 patients with FAP were given sulindac 150 mg orally twice a day. Polyp number and size were determined before treatment and at three

months. The relation of nine clin. factors to polyp regression (per cent of baseline polyp number after treatment) was evaluated by univariate and multivariate anal. Results-After three months of sulindac, polyp number had decreased to 45 per cent of baseline and polyp size to 50 per cent of baseline ($p < 0.001$ and $p < 0.01$, resp.). Univariate anal. showed greater polyp regression in older patients ($p = 0.004$), those with previous colectomy and ileorectal anastomosis ($p = 0.001$), and patients without identifiable mutation of the APC gene responsible for FAP ($p = 0.05$). With multivariate regression anal., response to sulindac treatment was associated with previous subtotal colectomy. Conclusions-Sulindac treatment seems effective in producing regression of colorectal adenomas of FAP patients with previous subtotal colectomy regardless of baseline polyp number and size. Changed sulindac metabolism, reduced area of the target mucosa, or changed epithelial characteristics after ileorectal anastomosis may explain these findings.

ST sulindac colorectal adenomas adenomatous polyposis

IT Neoplasm inhibitors
(large intestine, sulindac induced regression of colorectal adenomas in familial adenomatous polyposis in humans)

IT Intestine, neoplasm
(large, inhibitors, sulindac induced regression of colorectal adenomas in familial adenomatous polyposis in humans)

IT 38194-50-2, Sulindac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulindac induced regression of colorectal adenomas in familial adenomatous polyposis in humans)

=> d ibib abs kwic 2

L12 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:259707 CAPLUS

DOCUMENT NUMBER: 136:379639

TITLE: Primary chemoprevention of familial adenomatous polyposis with sulindac

AUTHOR(S): Giardiello, Francis M.; Yang, Vincent W.; Hyland,

Linda M.; Krush, Anne J.; Petersen, Gloria M.;
Trimbath, Jill D.; Piantadosi, Steven; Garrett,
Elizabeth; Geiman, Deborah E.; Hubbard, Walter;
Offerhaus, Johan A.; Hamilton, Stanley R.
CORPORATE SOURCE: Dep. Med., Johns Hopkins Univ. Sch. Med., Baltimore,
MD, USA
SOURCE: New England Journal of Medicine (2002), 346(14),
1054-1059
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Familial adenomatous polyposis is caused by a germ-line mutation in the adenomatous polyposis coli gene and is characterized by the development of hundreds of colorectal adenomas and, eventually, colorectal cancer. Nonsteroidal antiinflammatory drugs can cause regression of adenomas, but whether they can prevent adenomas is unknown. Methods: The authors conducted a randomized, double-blind, placebo-controlled study of 41 young subjects (age range, 8 to 25 yr) who were genotypically affected with familial adenomatous polyposis but phenotypically unaffected. The subjects received either 75 or 150 mg of sulindac orally twice a day or identical-appearing placebo tablets for 48 mo. The number and size of new adenomas and side effects of therapy were evaluated every four months for four years, and the levels of five major prostaglandins were serially measured in biopsy specimens of normal-appearing colorectal mucosa. Results: After four years of treatment, the average rate of compliance exceeded 76 % in the sulindac group, and mucosal prostaglandin levels were lower in this group than in the placebo group. During the course of the study, adenomas developed in 9 of 21 subjects (43 %) in the sulindac group and 11 of 20 subjects in the placebo group (55 %) ($P = 0.54$). There were no significant differences in the mean number ($P = 0.69$) or size ($P = 0.17$) of polyps between the groups. Sulindac did not slow the development of adenomas, according to an evaluation involving linear longitudinal methods. Conclusions: Standard doses of sulindac did not prevent the development of adenomas in subjects with familial adenomatous polyposis.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Background: Familial adenomatous polyposis is caused by a germ-line mutation in the adenomatous polyposis coli gene and is characterized by the development of hundreds of colorectal adenomas and, eventually, colorectal cancer. Nonsteroidal antiinflammatory drugs can cause regression of adenomas, but whether they can prevent adenomas is unknown. Methods: The authors conducted a randomized, double-blind, placebo-controlled study of 41 young subjects (age range, 8 to 25 yr) who were genotypically affected with familial adenomatous polyposis but phenotypically unaffected. The subjects received either 75 or 150 mg of sulindac orally twice a day or identical-appearing placebo tablets for 48 mo. The number and size of new adenomas and side effects of therapy were evaluated every four months for four years, and the levels of five major prostaglandins were serially measured in biopsy specimens of normal-appearing colorectal mucosa. Results: After four years of treatment, the average rate of compliance exceeded 76 % in the sulindac group, and mucosal prostaglandin levels were lower in this group than in the placebo group. During the course of the study, adenomas developed in 9 of 21 subjects (43 %) in the sulindac group and 11 of 20 subjects in the placebo group (55 %) ($P = 0.54$). There were no significant differences in the mean number ($P = 0.69$) or size ($P = 0.17$) of polyps between the groups. Sulindac did not slow the development of adenomas, according to an evaluation involving linear longitudinal methods. Conclusions: Standard doses of sulindac did not prevent the development of adenomas in subjects with familial adenomatous polyposis.

IT Prostaglandins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(colorectal mucosa prostaglandin levels as measure of

sulindac local effect in humans with familial adenomatous polyposis)
 IT Antitumor agents
 (colorectal, adenoma; primary chemoprevention of familial
 adenomatous polyposis with sulindac in humans)
 IT Intestine, neoplasm
 (colorectal, inhibitors, adenoma; primary chemoprevention of
 familial adenomatous polyposis with sulindac in humans)
 IT Intestine, neoplasm
 (familial polyposis; primary chemoprevention of familial adenomatous
 polyposis with sulindac in humans)
 IT Intestine
 (large, mucosa; colorectal mucosa prostaglandin levels as
 measure of sulindac local effect in humans with familial adenomatous
 polyposis)
 IT 363-24-6, Prostaglandin E2 551-11-1, Prostaglandin F2 α
 13367-85-6, Prostaglandin B2 41598-07-6, Prostaglandin D2 58962-34-8,
 6-keto-Prostaglandin F1 α
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (colorectal mucosa prostaglandin levels as measure of
 sulindac local effect in humans with familial adenomatous polyposis)
 IT 38194-50-2, Sulindac
 RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological
 activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (primary chemoprevention of familial adenomatous polyposis
 with sulindac in humans)

=> d his

(FILE 'HOME' ENTERED AT 09:22:46 ON 14 DEC 2005).

FILE 'REGISTRY' ENTERED AT 09:22:55 ON 14 DEC 2005

E "SULINDAC"/CN 25

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 09:23:34 ON 14 DEC 2005

L2 1426 S L1
 L3 254068 S GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLO
 L4 1099978 S CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?
 L5 65506 S L4 AND L3
 L6 234 S L5 AND L2
 L7 243958 S ORAL?
 L8 30 S L7 AND L6
 L9 186 S L2 (L) L4
 L10 121 S L9 AND L3
 L11 14 S L10 AND L7
 L12 9 S L11 NOT PY>2002

=> s lipsom? or microspher? or encapsulat? or polymer?

74 LIPSOM?
 27180 MICROSPHER?
 55572 ENCAPSULAT?
 1820552 POLYMER?
 84067 POLYMD
 84067 POLYMD
 (POLYMD)
 31147 POLYMG
 326031 POLYMN
 8505 POLYMNS
 327118 POLYMN
 (POLYMN OR POLYMNS)
 1885881 POLYMER?
 (POLYMER? OR POLYMD OR POLYMG OR POLYMN)
 L13 1945587 LIPSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?

=> s 113 and 112
L14 0 L13 AND L12

=> s 14 and 12
L15 443 L4 AND L2

=> s 19 and 113
L16 12 L9 AND L13

=> s 116 not py>2002
3346380 PY>2002
L17 3 L16 NOT PY>2002

=> d ibib 1-3

L17 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:430708 CAPLUS
DOCUMENT NUMBER: 135:236055
TITLE: Rat colorectal tumors treated with a range of
nonsteroidal anti-inflammatory drugs show altered
cyclooxygenase-2 and cyclooxygenase-1 splice variant
mRNA expression levels
AUTHOR(S): Vogliagis, Daphne; Brown, Wendy; Glare, Eric M.;
O'Brien, Paul E.
CORPORATE SOURCE: Department of Surgery, Monash University Medical
School, Alfred Hospital, Prahran, 3181, Australia
SOURCE: Carcinogenesis (2001), 22(6), 869-874.
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:457250 CAPLUS
DOCUMENT NUMBER: 129:76490
TITLE: Method for treating a tumor with a chemotherapeutic
agent and nonemulsified ultrapurified
polymerized hemoglobin solution
INVENTOR(S): Teicher, Beverly A.; Rausch, Carl W.; Hopkins, Robert
E., II
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA; Biopure Corp.
SOURCE: U.S., 16 pp., Cont.-in-part of U. S. Ser. No. 94,501.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5776898	A	19980707	US 1995-477110	19950607
US 5679638	A	19971021	US 1993-94501	19930720
PRIORITY APPLN. INFO.:			US 1991-699769	A2 19910514
			US 1993-94501	A2 19930720
REFERENCE COUNT:	59	THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L17 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:689536 CAPLUS
DOCUMENT NUMBER: 127:326520
TITLE: Method for treating a tumor with a chemotherapeutic
agent
INVENTOR(S): Teicher, Beverly A.; Rausch, Carl W.; Hopkins, Robert

PATENT ASSIGNEE(S): E., II
 SOURCE: Biopure Corporation, USA; Dana Farber Cancer Institute
 U.S., 12 pp., Cont.-in-part of U.S. Ser. No.
 699,769, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5679638	A	19971021	US 1993-94501	19930720
US 5776898	A	19980707	US 1995-477110	19950607
PRIORITY APPLN. INFO.:			US 1991-699769	B2 19910514
			US 1993-94501	A2 19930720

=> d ibib abs kwic 1

L17 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:430708 CAPLUS

DOCUMENT NUMBER: 135:236055

TITLE: Rat colorectal tumors treated with a range of
 nonsteroidal anti-inflammatory drugs show altered
 cyclooxygenase-2 and cyclooxygenase-1 splice variant
 mRNA expression levels

AUTHOR(S): Vogliagis, Daphne; Brown, Wendy; Glare, Eric M.;
 O'Brien, Paul E.

CORPORATE SOURCE: Department of Surgery, Monash University Medical
 School, Alfred Hospital, Prahran, 3181, Australia

SOURCE: Carcinogenesis (2001), 22(6), 869-874

CODEN: CRNGDP; ISSN: 0143-3334

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce tumor mass by
 increasing tumor cell apoptosis and decreasing cell proliferation. The
 classically recognized targets for NSAID action are the two isoforms of
 the cyclooxygenase (COX) gene, which is responsible for prostaglandin
 production. In the rat, the COX-1 gene expresses an alternatively spliced mRNA
 COX-1 splice variant (SV) which may, at best, code for a truncated COX-1
 protein. Previously, it was reported that COX-1SV mRNA is differentially
 expressed in the ageing stomach. In this study, carcinogen-treated rats
 were treated for 23 wk with the NSAIDs celecoxib, sulindac or sulindac
 sulfone, while untreated rats received vehicle alone. The nos. and vols.
 of tumor per animal were recorded and histol. was performed. The
 competitive polymerase chain reaction, was used to determine whether
 COX gene expression was altered in colorectal tumors and in regions of
 adjacent and distant macroscopically normal intestine, from vehicle- or
 NSAID-treated rats. In addition, COX-1 and COX-2 were immunolocalized in the
 same tumor and normal colonic tissue. Tumors from animals treated with
 vehicle or celecoxib expressed elevated levels of COX-2 mRNA in comparison
 with the adjacent normal mucosa. In contrast, tumors from sulindac- and
 sulindac sulfone-treated rats expressed less COX-2 mRNA than tumors from
 vehicle-treated rats. The expression of COX-1 mRNA remained unchanged in
 all tissues examined. However, COX-1SV mRNA contents were elevated in
 colorectal tumors and reduced after NSAID treatment to the values in
 normal colonic mucosa. The results indicate that the antineoplastic
 actions of NSAIDs may be attributed to COX-dependent and/or
 COX-independent mechanisms of action. The presence and differential
 expression of COX-1SV mRNA was also demonstrated in colon tumors. COX-1SV
 mRNA represents 2% of the total COX-1 mRNA expressed and its role in colon
 cancer remains to be established.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Nonsteroidal anti-inflammatory drugs (NSAIDs) reduce tumor mass by increasing tumor cell apoptosis and decreasing cell proliferation. The classically recognized targets for NSAID action are the two isoforms of the cyclooxygenase (COX) gene, which is responsible for prostaglandin production. In the rat, the COX-1 gene expresses an alternatively spliced mRNA COX-1 splice variant (SV) which may, at best, code for a truncated COX-1 protein. Previously, it was reported that COX-1SV mRNA is differentially expressed in the ageing stomach. In this study, carcinogen-treated rats were treated for 23 wk with the NSAIDs celecoxib, sulindac or sulindac sulfone, while untreated rats received vehicle alone. The nos. and vols. of tumor per animal were recorded and histol. was performed. The competitive polymerase chain reaction, was used to determine whether COX gene expression was altered in colorectal tumors and in regions of adjacent and distant macroscopically normal intestine, from vehicle- or NSAID-treated rats. In addition, COX-1 and COX-2 were immunolocalized in the same tumor and normal colonic tissue. Tumors from animals treated with vehicle or celecoxib expressed elevated levels of COX-2 mRNA in comparison with the adjacent normal mucosa. In contrast, tumors from sulindac- and sulindac sulfone-treated rats expressed less COX-2 mRNA than tumors from vehicle-treated rats. The expression of COX-1 mRNA remained unchanged in all tissues examined. However, COX-1SV mRNA contents were elevated in colorectal tumors and reduced after NSAID treatment to the values in normal colonic mucosa. The results indicate that the antineoplastic actions of NSAIDs may be attributed to COX-dependent and/or COX-independent mechanisms of action. The presence and differential expression of COX-1SV mRNA was also demonstrated in colon tumors. COX-1SV mRNA represents 2% of the total COX-1 mRNA expressed and its role in colon cancer remains to be established.

IT 38194-50-2, Sulindac 59973-80-7, Sulindac sulfone 169590-42-5, Celecoxib

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(colorectal tumors treated with nonsteroidal anti-inflammatory drugs show altered cyclooxygenase-2 and cyclooxygenase-1 splice variant mRNA expression)

=> file medline

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	64.77	70.01
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.65	-3.65

FILE 'MEDLINE' ENTERED AT 09:35:28 ON 14 DEC 2005

FILE LAST UPDATED: 8 DEC 2005 (20051208/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

<http://www.nlm.nih.gov/mesh/>
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the

MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s SULINDAC/CN

L18 919 SULINDAC/CN

=> s cancer? or tumor? or neoplas? or polyp?

547932 CANCER?

758323 TUMOR?

1455946 NEOPLAS?

155044 POLYP?

L19 1879233 CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?

=> s gastrointestinal or esophag? or gastic? or intestin? or colorect?

1 GASTROINTESTINAL

101857. ESOPHAG?

50 GASTIC?

293936 INTESTIN?

45036 COLORECT?

L20 428581 GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLORECT?

=> s l19 and l20

L21 125328 L19 AND L20

=> s l21 and l18

L22 175 L21 AND L18

=> s liposom? or microspher? or encapsulat? or polymer?

30623 LIPOSOM?

21357 MICROSPHER?

15072 ENCAPSULAT?

351141 POLYMER?

L23 407843 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?

=> s l23 and l22

L24 8 L23 AND L22

=> s l24 not py>2002

1733376 PY>2002

L25 6 L24 NOT PY>2002

=> d ibib 1-3

L25 ANSWER 1 OF 6 MEDLINE on STN

ACCESSION NUMBER: 2002696841 MEDLINE

DOCUMENT NUMBER: PubMed ID: 12458338

TITLE: Effects of long-term administration of sulindac on APC mRNA and apoptosis in colons of rats treated with azoxymethane.

AUTHOR: Kishimoto Y; Yashima K; Morisawa T; Ohishi T; Marumoto A; Sano A; Idobe-Fujii Y; Miura N; Shiota G; Murawaki Y; Hasegawa J

CORPORATE SOURCE: Division of Pharmacotherapeutics, Department of Pathophysiological and Therapeutic Science, Faculty of Medicine, Tottori University, 86 Nishicho, Yonago 683-8503, Japan.. ykishimo@grape.med.tottori-u.ac.jp

SOURCE: Journal of cancer research and clinical oncology, (2002 Nov) 128 (11) 589-95. Electronic Publication: 2002-10-04. Journal code: 7902060. ISSN: 0171-5216.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030118
Entered Medline: 20030117

L25 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001065648 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11093808
TITLE: Growth-suppressive effect of non-steroidal
anti-inflammatory drugs on 11 colon-cancer cell
lines and fluorescence differential display of genes whose
expression is influenced by sulindac.
AUTHOR: Akashi H; Han H J; Iizaka M; Nakamura Y
CORPORATE SOURCE: Laboratory of Molecular Medicine, Human Genome Center,
Institute of Medical Science, University of Tokyo, Tokyo,
Japan.
SOURCE: International journal of cancer. Journal international du
cancer, (2000 Dec 15) 88 (6) 873-80.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222

L25 ANSWER 3 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2001064500 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11076880
TITLE: Sulindac and a cyclooxygenase-2 inhibitor, etodolac,
increase APC mRNA in the colon of rats treated with
azoxymethane.
AUTHOR: Kishimoto Y; Takata N; Jinnai T; Morisawa T; Shiota G;
Kawasaki H; Hasegawa J
CORPORATE SOURCE: Department of Clinical Pharmacology, Faculty of Medicine,
Tottori University, 86 Nishicho, Yonago 683-8503, Japan..
ykishimo@grape.med.tottori-u.ac.jp
SOURCE: Gut, (2000 Dec) 47 (6) 812-9.
Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001222

=> d ibib 4-6

L25 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2000295032 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10833474
TITLE: Par-4, a proapoptotic gene, is regulated by NSAIDs in human
colon carcinoma cells.
AUTHOR: Zhang Z; DuBois R N
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine and
Cell Biology, Vanderbilt University Medical Center,
Veterans Affairs Medical Center, Nashville, Tennessee, USA.
CONTRACT NUMBER: DK47297 (NIDDK)
P30 CA68485 (NCI)
PO CA77839 (NCI)

SOURCE: Gastroenterology, (2000 Jun) 118 (6) 1012-7.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000629
Last Updated on STN: 20021219
Entered Medline: 20000621

L25 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 1999333404 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10403841
TITLE: Redistribution of activated caspase-3 to the nucleus during
butyric acid-induced apoptosis.
AUTHOR: Mandal M; Adam L; Kumar R
CORPORATE SOURCE: Cell Growth Regulation Laboratory, University of Texas M.D.
Anderson Cancer Center, Houston, Texas, 77030, USA.
SOURCE: Biochemical and biophysical research communications, (1999
Jul 14) 260 (3) 775-80.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 20020420
Entered Medline: 19990816

L25 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 96334961 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8707116
TITLE: Sulindac increases the expression of APC mRNA in malignant
colonic epithelial cells: an in vitro study.
AUTHOR: Schnitzler M; Dwight T; Robinson B G
CORPORATE SOURCE: Molecular Genetics Unit, Kolling Institute of Medical
Research, Royal North Shore Hospital, St Leonards, NSW,
Australia.
SOURCE: Gut, (1996 May) 38 (5) 707-13.
Journal code: 2985108R. ISSN: 0017-5749.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960919
Last Updated on STN: 19970203
Entered Medline: 19960910

=> d ibib abs kwic 4

L25 ANSWER 4 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2000295032 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10833474
TITLE: Par-4, a proapoptotic gene, is regulated by NSAIDs in human
colon carcinoma cells.
AUTHOR: Zhang Z; DuBois R N
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine and
Cell Biology, Vanderbilt University Medical Center,
Veterans Affairs Medical Center, Nashville, Tennessee, USA.
CONTRACT NUMBER: DK47297 (NIDDK)
P30 CA68485 (NCI)

PO CA77839 (NCI)

SOURCE: Gastroenterology, (2000 Jun) 118 (6) 1012-7.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000629
Last Updated on STN: 20021219
Entered Medline: 20000621

AB BACKGROUND & AIMS: Many reports indicate that nonsteroidal anti-inflammatory drugs (NSAIDs) have antineoplastic effects, but the precise molecular mechanism(s) responsible are unclear. We evaluated the effect of cyclooxygenase (COX) inhibitors (NSAIDs) on human colon carcinoma cells (HCA-7) and identified several genes that are regulated after treatment with NS-398, a selective COX-2 inhibitor. METHODS: Differential display polymerase chain reaction cloning techniques were used to identify genes regulated by treatment with NSAIDs and selective COX-2 inhibitors. RESULTS: A prostate apoptosis response 4 (Par-4) gene was up-regulated after NSAID treatment. Par-4 was first isolated from prostate carcinoma cells undergoing apoptosis, and expression of Par-4 sensitized cancer cells to apoptotic stimuli. Par-4 levels were increased in cells treated with COX inhibitors such as NS-398, nimesulide, SC-58125, and sulindac sulfide. Treatment of HCA-7 cells with these agents also induced apoptotic cell death. CONCLUSIONS: The results suggest that regulation of Par-4 contributes to the proapoptotic effects of high-dose COX inhibitors (NSAIDs) by serving as a downstream mediator leading to initiation of programmed cell death.

AB . . . cells (HCA-7) and identified several genes that are regulated after treatment with NS-398, a selective COX-2 inhibitor. METHODS: Differential display polymerase chain reaction cloning techniques were used to identify genes regulated by treatment with NSAIDs and selective COX-2 inhibitors. RESULTS: A . . . was up-regulated after NSAID treatment. Par-4 was first isolated from prostate carcinoma cells undergoing apoptosis, and expression of Par-4 sensitized cancer cells to apoptotic stimuli. Par-4 levels were increased in cells treated with COX inhibitors such as NS-398, nimesulide, SC-58125, and. . .

CT . . . pharmacology
*Apoptosis: DE, drug effects
Apoptosis: GE, genetics
Blotting, Northern
Blotting, Western
Carrier Proteins: AN, analysis
*Carrier Proteins: GE, genetics
Colonic Neoplasms
Cyclooxygenase Inhibitors: PD, pharmacology
DNA Fragmentation
Gene Expression: DE, drug effects
Gene Expression: PH, physiology
Humans
Intestinal Mucosa: CH, chemistry
*Intestinal Mucosa: CY, cytology
Intestinal Mucosa: EN, enzymology
*Intracellular Signaling Peptides and Proteins
*Nitrobenzenes: PD, pharmacology
Protein Kinase C: ME, metabolism
Pyrazoles: PD, pharmacology
. . . Support, U.S. Gov't, Non-P.H.S.
. . . Research Support, U.S. Gov't, P.H.S.
*Sulfonamides: PD, pharmacology
Sulindac: AA, analogs & derivatives
Sulindac: PD, pharmacology
Tumor Cells, Cultured

RN 123653-11-2 (N-(2-cyclohexyloxy-4-nitrophenyl)methanesulfonamide);

162054-19-5 (1-((4-methylsulfonyl)phenyl)-3-trifluoromethyl-5-(4-fluorophenyl)pyrazole); 32004-67-4 (sulindac sulfide); 38194-50-2 (Sulindac); 51803-78-2 (nimesulide)

=> d his

(FILE 'HOME' ENTERED AT 09:22:46 ON 14 DEC 2005)

FILE 'REGISTRY' ENTERED AT 09:22:55 ON 14 DEC 2005

E "SULINDAC"/CN 25

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 09:23:34 ON 14 DEC 2005

L2 1426 S L1
L3 254068 S GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLO
L4 1099978 S CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?
L5 65506 S L4 AND L3
L6 234 S L5 AND L2
L7 243958 S ORAL?
L8 30 S L7 AND L6
L9 186 S L2 (L) L4
L10 121 S L9 AND L3
L11 14 S L10 AND L7
L12 9 S L11 NOT PY>2002
L13 1945587 S LIPSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?
L14 0 S L13 AND L12
L15 443 S L4 AND L2
L16 12 S L9 AND L13
L17 3 S L16 NOT PY>2002

FILE 'MEDLINE' ENTERED AT 09:35:28 ON 14 DEC 2005

L18 919 S SULINDAC/CN
L19 1879233 S CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?
L20 428581 S GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLO
L21 125328 S L19 AND L20
L22 175 S L21 AND L18
L23 407843 S LIPOSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?
L24 8 S L23 AND L22
L25 6 S L24 NOT PY>2002

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	3.52	73.53
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.65

FILE 'CAPLUS' ENTERED AT 09:38:57 ON 14 DEC 2005

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=> s liposom? or microspher? or encapsulat? or polymer?

48683 LIPOSOM?
27180 MICROSPHER?
55572 ENCAPSULAT?
1820552 POLYMER?
84067 POLYMD
84067 POLYMD
(POLYMD)
31147 POLYMG
326031 POLYMN
8505 POLYMNS
327118 POLYMN
(POLYMN OR POLYMNS)
1885881 POLYMER?
(POLYMER? OR POLYMD OR POLYMG OR POLYMN)

L26 1984458 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT? OR POLYMER?

=> s 19 and 126

L27 15 L9 AND L26

=> s liposom? or microspher? or encapsulat?

48683 LIPOSOM?
27180 MICROSPHER?
55572 ENCAPSULAT?

L28 122087 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT?

=> s 128 and 19

L29 11 L28 AND L9

=> s 129 not py>2002

3346380 PY>2002

L30 0 L29 NOT PY>2002

=> s 129 not py>2003

2266400 PY>2003

L31 0 L29 NOT PY>2003

=> d 129 ibib 1-4

L29 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:591975 CAPLUS

DOCUMENT NUMBER: 143:53482

TITLE: Method for inhibiting the growth of gastrointestinal tract tumors

INVENTOR(S): Egilmez, Nejat K.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 21 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147689	A1	20050707	US 2003-748003	20031230

CA 2491338 AA 20050630 CA 2004-2491338 20041223
PRIORITY APPLN. INFO.: US 2003-748003 A 20031230

L29 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:14227 CAPLUS
DOCUMENT NUMBER: 142:107439
TITLE: Cardiolipin synthesis inhibitor for treatment of
cardiovascular disorders, and obesity
INVENTOR(S): Jamil, Haris; Ahmad, Moghis U.; Ahmad, Imran
PATENT ASSIGNEE(S): Neopharm, Inc., USA
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000318	A2	20050106	WO 2004-US20104	20040623
WO 2005000318	A3	20050414		
WO 2005000318	B1	20050526		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2003-480669P P 20030623

L29 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:877933 CAPLUS
DOCUMENT NUMBER: 141:365149
TITLE: Anti-PSGL-1 antibodies and scFv fragments for
diagnosis, prognosis and therapy of cancer,
metastasis, autoimmune disease and inflammation
INVENTOR(S): Levanon, Avigdor; Ben-Levy, Rachel; Plaksin, Daniel;
Szanton, Esther; Hagai, Yocheved; Mar-Chaim, Hagit
Hoch
PATENT ASSIGNEE(S): Israel
SOURCE: U.S. Pat. Appl. Publ., 49 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004208877	A1	20041021	US 2003-611588	20030630
PRIORITY APPLN. INFO.:			US 2002-393491P	P 20020701

L29 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:856929 CAPLUS
DOCUMENT NUMBER: 141:348831
TITLE: Antibodies specific to epitopes involving cell
rolling, metastasis and inflammation for treatment of
tumor, restenosis, thrombosis, autoimmune disease and
inflammation
INVENTOR(S): Lazarovits, Janette; Nimrod, Abraham; Hoch, Mar-Chaim

PATENT ASSIGNEE(S): Hagit; Levanon, Avigdor
 SOURCE: Israel
 U.S. Pat. Appl. Publ., 22 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004202665	A1	20041014	US 2003-610843	20030630
PRIORITY APPLN. INFO.:			US 2002-393453P	P 20020701

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 COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
23.21	96.74

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE ENTRY	TOTAL SESSION
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=> s SULINDAC
 L32 2826 SULINDAC

=> s 132/ab
 L33 9 (SULINDAC/AB)

=> s cancer? or tumor? or neoplas? or polyp?
 73935 CANCER?
 61948 TUMOR?
 21353 NEOPLAS?
 153344 POLYP?
 L34 196562 CANCER? OR TUMOR? OR NEOPLAS? OR POLYP?

=> s 134 and 133
 L35 7 L34 AND L33

=> s gastrointestinal or esophag? or gastic? or intestin? or colorect?
 4 GASTROINTESTINAL
 11126 ESOPHAG?
 83 GASTIC?
 38774 INTESTIN?
 8423 COLORECT?
 L36 47131 GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLOREC
 T?

=> s gastrointestinal or esophag? or gastic? or intestin? or colorect?
 28847 GASTROINTESTINAL

9 GASTROINTESTINALS
 28851 GASTROINTESTINAL
 (GASTROINTESTINAL OR GASTROINTESTINALS)
 11126 ESOPHAG?
 83 GASTIC?
 38774 INTESTIN?
 8423 COLORECT?
 L37 59284 GASTROINTESTINAL OR ESOPHAG? OR GASTIC? OR INTESTIN? OR COLORECT
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=> s 137 and 135
 L38 7 L37 AND L35

=> s liposom? or microspher? or encapsulat?
 40590 LIPOSOM?
 15203 MICROSPHER?
 61501 ENCAPSULAT?
 L39 90511 LIPOSOM? OR MICROSPHER? OR ENCAPSULAT?

=> s 139 and 138
 L40 2 L39 AND L38

=> d ibib 1-2

L40 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 2001035956 PCTFULL ED 20020820
 TITLE (ENGLISH): USE OF NSAIDS FOR THE TREATMENT OF PANCREATIC
 CANCER
 TITLE (FRENCH): UTILISATION DES AINS DANS LE TRAITEMENT DU
 CANCER DU PANCREAS
 INVENTOR(S): MARSHALL, Mark, Steven;
 SWEENEY, Christopher, J.;
 YIP-SCHNEIDER, Michelle, T.;
 CROWELL, Pamela, L.
 PATENT ASSIGNEE(S): ADVANCED RESEARCH AND TECHNOLOGY INSTITUTE, INC.;
 MARSHALL, Mark, Steven;
 SWEENEY, Christopher, J.;
 YIP-SCHNEIDER, Michelle, T.;
 CROWELL, Pamela, L.
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2001035956	A1	20010525

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
 CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US31410 A 20001115
 PRIORITY INFO.: US 1999-60/165,543 19991115

L40 ANSWER 2 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 1999049859 PCTFULL ED 20020515
 TITLE (ENGLISH): DFMO AND SULINDAC COMBINATION IN CANCER
 CHEMOPREVENTION
 TITLE (FRENCH): COMBINAISON DE DFMO ET DE SULINDAC DANS LA
 CHIMIOPREVENTION DU CANCER
 INVENTOR(S): GERNER, Eugene, W.;
 MEYSKENS, Frank, L., Jr.
 PATENT ASSIGNEE(S): THE ARIZONA BOARD OF REGENTS on behalf of THE

UNIVERSITY OF ARIZONA;
 THE REGENTS OF THE UNIVERSITY OF CALIFORNIA;
 GERNER, Eugene, W.;
 MEYSKENS, Frank, L., Jr.
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9949859	A1	19991007

DESIGNATED STATES

W:

AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
 KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL
 PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN
 YU ZA ZW GH GM KE LS MW SD SL SZ UG ZW AM AZ BY KG KZ
 MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU
 MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD
 TG

APPLICATION INFO.: WO 1999-US6693 A 19990326
 PRIORITY INFO.: US 1998-60/079,850 19980328

=> d kwic 1

L40 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
 TIEN USE OF NSAIDS FOR THE TREATMENT OF PANCREATIC CANCER
 TIFR UTILISATION DES AINS DANS LE TRAITEMENT DU CANCER DU PANCREAS
 ABEN The invention provides a method comprising the use of non-steroidal
 antiinflammatory drugs (NSAIDs), particularly sulindac or its
 analogs to treat pancreatic cancer.

DETD USE OF NSAIDS FOR THE TREATMENT OF PANCREATIC CANCER
 Background of the Invention
 Cancer of the pancreas ranks 'ust behind lung cancer
 , colon cancer, and
 breast cancer as the most common cause of death by
 cancer (1). It is more
 common among men, and men between the ages of 60 and 70 are most at
 risk.

The cause of pancreatic cancer is unknown.

which are not fully understood, usually is
 1 0 significant. The average loss is about 25 pounds. Jaundice occurs if
 the cancer
 blocks the common bile duct. The survival rate with pancreatic
 cancer is poor.

By the time the malignant tumor is identified, it often has
 spread (metastasized)
 to other parts of the body. The median survival is little more than six.

5 Often the tumor cannot be removed by surgery, either because
 it has
 invaded vital structures that cannot be removed or because it has spread
 to
 distant sites. Chemotherapy and radiation therapy can be used on the
 tumor,
 although these treatments often are not beneficial.

Easton, PA (18th ed., 1990) at pages
 1115

There is a large amount of literature on the effect of NSAIDs on

cancer,
particularly colon cancer. For example, see H. A. Weiss et al., Scand J.

in vitro, but that
indomethacin, ketoralac and NS-398, did not. Sulindac has been investigated in
combination therapy for the treatment of colon cancer. See, H. M. Verheul et al.,
Brit- J. Cance , 79, 114 (1999); F. A. Sinicrope et al., Clin. Cancer Res-, 2, 37
(1996); and M. Mooghen et al., J. Pathol., LI]6, 394 (1988).

C. P. Duffy et al., Eur. J. Cancer, 34, 1250 (1998), reported that the
cytotoxicity of certain chemotherapeutic drugs was enhanced when they were
combined with certain non-steroidal anti-inflammatory agents. The effects
observed against human lung cancer cells and human leukemia cells were highly
specific and not predictable; i.e., some combinations of NSAID and agent were
effective and some. . . .

a PCT application (WO98/18490) on October 24,
1997, directed to a combination of a substrate for MRP, which can be an anti-
cancer drug, and a NSAID that increases the potency of the anti-cancer drug.

Therefore, a continuing need exists for methods to control cancers, and to
increase the potency of anti-cancer drugs with relatively non-toxic agents.

Summary of the Invention

In one aspect, the present invention provides a therapeutic method to treat
pancreatic cancer, comprising administering to a mammal afflicted with
pancreatic cancer an amount of a NSAID, preferably sulindac ((Z) fluoro
methyl-1-[[4-(methylsulfinyl)phenyl] methylene]-1H-Indene acetic acid),
or
an analog thereof, preferably one that is a COX-2 inhibitor, effective to inhibit
the viability of pancreatic cancer cells of said mammal. The present invention
also provides a method of increasing the susceptibility of human pancreatic
cancer cells to a chemotherapeutic agent comprising contacting the cells with an
effective sensitizing amount of a NSAID, preferably sulindac, or said analog
thereof. Thus, the invention provides a therapeutic method for the treatment of a
human or other mammal afflicted with pancreatic cancer, wherein an effective
amount of an NSAID, preferably sulindac or said analog thereof is administered
to a subject afflicted with pancreatic cancer and undergoing treatment with a
5 chemotherapeutic (antineoplastic) agent.

Preferably, sulindac is administered in conjunction with one or more chemotherapeutic agents effective against pancreatic cancer such as gemcitabine or 5-FU.

A method of evaluating the ability of sulindac to sensitize pancreatic cancer cells to a chemotherapeutic agent is also provided. The assay method

comprises: (a) isolating a first portion of pancreatic cancer cells from a human

cancer patient; (b) measuring their viability; (c) administering sulindac, or said

analog thereof, to said patient; (d) isolating a second portion of pancreatic cancer

cells from said patient; (e) measuring the viability of the second portion of

pancreatic cancer cells; and (f) comparing the viability measured in step (e) with

the viability measured in step (b); wherein reduced viability in. . .

(b) and (e) are carried out in the presence of the chemotherapeutic agent, as will be the case when the pancreatic cancer cells are derived from the blood of a mammal afflicted with pancreatic cancer.

Thus, a cancer patient about to undergo, or undergoing, treatment for

pancreatic cancer can be rapidly evaluated to see if he/she will benefit from

concurrent chemotherapy and administration of sulindac or an analog thereof.

Description of the Figures

Figure 1. Photocopy of a representative immunoblot of pancreatic adenocarcinomas and matched normal tissue. Lysates were prepared from tumor

(T) specimens obtained from six patients, three with matched normal (N) tissue

(sample numbers correspond to those listed in Table 1). Lysates. . . expresses neither COX- I or COX

Figure 2. Percent COX-2 expression in patient samples. Values of % COX-2 expression for all tumor samples, shown by solid circles, and non-nal

tissue, shown by open circles, from Table I are plotted. Values for mean, median

and range are indicated. The % COX-2 expression for the matched pancreatic

tumor/normal tissue sets is shown in the inset (n = 11).

Lines are drawn between

the corresponding tumor values, shown by solid circles, and non-nal values,

shown by the open circles. The difference in COX-2 expression between tumor

and non-nal specimens was determined to be statistically significant (P = 0.004).

Figure 3. COX-2 expression in pancreatic tumor cell lines. A) COX-2

expression in human pancreatic cell lines detected by immunoblot analysis. The

K-ras mutation status of each of the. . .

Figure 4. Effect of COX inhibitors on the growth of pancreatic tumor

cell lines. The cell lines BxPC-3, shown by the black bars, and PaCa-2, shown by the hatched bars, were plated in the. . .

Figure 5. Prostaglandin E2 production. A) PGE2 levels in pancreatic tumor cell lines. Following incubation of exponentially growing cells with 15 μ M arachidonic acid in serum-free media for one hour, PGE2 levels.

Figure 6 is a graph depicting the effect of a combination of sulindac and gemcitabine on the growth of pancreatic tumor cell line BxPC.

Figure 7 is a graph depicting the effect of a combination of sulindac and gemcitabine on the growth of pancreatic tumor cell line PaCa

Detailed Description of the Invention

Difficulty in achieving early diagnosis as well as the aggressive nature of pancreatic cancer contribute to the low survival rate of patients with pancreatic cancer. Since few options exist for the treatment of pancreatic cancer, it is important to identify potential targets for drug therapy. In an effort to gain more insight into pancreatic tumorigenesis] pancreatic tumors have been analyzed at the molecular level to detect genetic lesions. Activating mutations within the K-ras gene have been detected in up to 90% of pancreatic carcinomas, suggesting that activation of the Ras pathway is important in the development of pancreatic cancer (2). Experimental chemotherapeutic strategies for pancreatic cancer patients currently include drugs which target the Ras signal transduction pathway.

For example, epidemiological studies have shown that prolonged use of aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) can reduce the risk of colon cancer by 40-50% (3). NSAIDs also inhibit chemically induced colon carcinomas in animal model systems (4). Since NSAIDs are known to inhibit cyclooxygenase. . . esters, and growth factors (5, 6). COX-2 expression has recently been shown to be elevated in several different types of human cancer, suggesting that the presence of COX-2 correlates with cancer development (7-11). Additional studies which directly link COX-2 to carcinogenesis include observations that human colon cancer cells expressing COX-2 acquire increased invasiveness (12) and that COX-2 expressed in intestinal epithelial cells inhibits apoptosis (13). COX-2 expression in colon cancer cells has also been found to promote angiogenesis of co-cultured endothelial cells by stimulating the production of angiogenic factors (14). Furthermore, direct genetic

evidence linking COX-2 to colorectal tumorigenesis was provided by a mouse model for human familial adenomatous polyposis (FA-P), an inherited condition leading to colorectal cancer; in this system, COX-2 gene knockouts and a specific COX-2 inhibitor were found to reduce the number of intestinal polyps formed (15).

The presence of oncogenic Ras has been associated with the induction of COX-2 expression in H-ras-transformed rat intestinal and mammary epithelial cells as well as in non-small cell lung cancer cell lines (16-18). To our knowledge, the association between oncogenic Ras and COX-2 expression has not been explored in vivo. The high frequency of activating mutations within the K-ras gene in pancreatic tumors should enable us to investigate the relationship between oncogenic K-ras and COX-2 expression in vivo. In the present study, we evaluated COX-2 protein levels in primary human pancreatic adenocarcinomas. We further examined whether COX-2 expression correlated with K-ras mutation status in pancreatic tumors as well as in pancreatic cancer cell lines. In light of our data demonstrating elevated levels of COX-2 protein in primary pancreatic tumors and cell lines, we tested the effect of the COX inhibitors sulindac, indomethacin and NS-398 on cell growth and prostaglandin E2 production in human pancreatic tumor cell lines.

Cyclooxygenase-2 (COX-2) expression is upregulated in several types of human cancers and has also been directly linked to carcinogenesis. To investigate the role of COX-2 in pancreatic cancer, we evaluated COX-2 protein expression in primary human pancreatic adenocarcinomas (n = 23) and matched normal adjacent tissue (n = 11) by immunoblot analysis. COX-2 expression was found to be significantly elevated in the pancreatic tumor specimens compared to normal pancreatic tissue. To examine whether the elevated levels of COX-2 protein observed in pancreatic tumors correlated with the presence of oncogenic K-ras, we determined the K-ras mutation status in a subset of the tumors and corresponding non-tumoral tissues. The presence of oncogenic K-ras did not correlate with the level of COX-2 protein expressed in the pancreatic adenocarcinomas analyzed. These observations were also confirmed in a panel of human pancreatic tumor cell lines. Furthermore, in the pancreatic tumor cell line expressing the highest level of COX-2 (BxPC-3), COX-2 expression was demonstrated to be independent of Erk1/2 Map kinase activation. The lack of correlation between COX-2 and oncogenic K-ras expression suggests that Ras activation may not be sufficient to inducing COX-2 expression in pancreatic

tumor cells and that the aberrant activation of signaling pathways other than Ras may be required for up-regulating COX-2 expression. We also report that the COX inhibitors sulindac, indomethacin, and NS-398 inhibited cell growth in both COX positive (BxPC-3) and COX negative (PaCa-2) pancreatic tumor cell lines. However, suppression of cell growth by indomethacin and NS-398 was significantly greater in the BxPC-3 cell line compared to. . . that COX-2 may play an important role in pancreatic tumorigenesis and therefore be a promising chemotherapeutic target for the treatment of pancreatic cancer.

I 0

Other NSAIDs, including indomethacin and NS-398 also the growth of pancreatic tumor cell lines, as discussed hereinbelow, and can also be used in the present method, alone, or preferably in combination with sulindac.

or infusion in dosages of about 500-4000 Mg/M² /week for up to 7 weeks/cycle for treatment of localized or metastatic pancreatic cancer (adenocarcinoma of the pancreas). It can also be administered in conjunction with other anti-cancer agents, such as 5-FU. See, PDR (53rd ed., 1999) at pages 1578

The effect of sulindac or NS-398 alone and in combination with gemcitabine on the growth of pancreatic tumor cells BxPC-3 and PaCa-2 was investigated. Treatment with the drug combinations inhibited the growth of both cell lines to a greater extent. . . NF-KB DNA binding activity was inhibited by parthenolide treatment. These results suggest that anti-inflammatory drugs may enhance the effectiveness of gemcitabine against pancreatic tumors.

of a prophylactic or therapeutic dose of sulindac, an analog thereof or a combination thereof, in the acute or chronic management of

cancer, i.e., pancreatic cancer, will vary with the stage of the cancer, such as the solid tumor to be treated, the chemotherapeutic agent(s) or other anti-cancer therapy used, and the route of administration. The dose, and perhaps the dose frequency, will also vary according to the age, body. . .

5 chemotherapy regimen. The sulindac, in some cases, may be combined with the same carrier or vehicle used to deliver the anti-cancer chemotherapeutic agent.

sterile powders comprising the active ingredient which are adapted for the extemporaneous preparation of sterile injectable or infusible solutions or dispersions, optionally encapsulated in liposomes. In all cases, the ultimate dosage form must be

sterile, fluid and stable under the conditions of manufacture and storage. The . . . like), vegetable oils, non-toxic glyceryl esters, and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the formation of liposomes, by the maintenance of the required particle size in the case of dispersions or by the use of surfactants. The prevention. . .

were obtained from the Indiana University Tissue Procurement Laboratory and the Cooperative Human Tissue Network (CHTN) which is funded by the National Cancer Institute. A total of 23 primary human pancreatic cancer specimens were analyzed in this study.

within 1 hour of surgical removal and subsequently stored at -80°C. Paraffin sections were prepared from a subset of the specimens. All tumor specimens used in this study were examined by a pathologist and classified as primary pancreatic adenocarcinomas.

5. Statistical Analysis. The presence of statistically significant elevation of COX-2 protein between cancer specimens and corresponding normal adjacent tissues was determined by the nonparametric signed rank test. A two-way analysis of variance (ANOVA) was used. . .

6. Cell Lines. The human pancreatic tumor cell lines (AsPC-1, BxPC-3, Capan-1, Capan-2, HPA-F-11, Hs766T, PaCa-2 and PANC-1) were obtained from the American Type Culture Collection (ATCC, Rockville, MD). . .

Undetectable levels of COX-2 protein were observed in each of the normal specimens. In contrast, COX-2 protein expression in the pancreatic 5 tumor tissues ranged from undetectable (sample #21) to slight/moderate (samples #12, 14, 20) to high levels (samples #9, 22). COX-1 protein was observed in both pancreatic tumor and normal tissues, although the level of expression was variable and not consistently elevated in the tumor specimens (Figure 1). Similar levels of p21 and actin expression were found in both the tumor and corresponding normal tissues (Figure 1).

narrower range (0-3%) of COX-2 expression in the normal tissues. Both the mean and median COX-2 expression were higher in the tumor samples, suggesting that COX-2 expression is elevated in pancreatic adenocarcinomas compared to normal tissue. The difference in COX-2 expression between the pancreatic tumor and corresponding normal tissue was determined to be statistically significant ($P = 0.004$) (Figure 2, inset).

less than 5% respectively, which

corresponds closely with visual detection in the immunoblots. According to these criteria, 6 out of 11 (55%) tumor samples in the matched tissue sets were COX-2 positive. Similarly, 13 out of the 23 (56%) total tumor specimens analyzed were COX-2 positive; in contrast, all the normal tissue samples (n = 11) were COX-2 negative.

Immunohistochemical staining of the pancreatic tumor specimens demonstrated that COX-2 expression was localized to the carcinoma cells and was not detectable in the stromal compartment of the tumors (Figure 3).

Example 2

COX-2 expression and K-ras mutation in pancreatic tumors and cell lines

To determine if COX-2 expression levels correlated with the K-ras mutation status of the tumors, genomic DNA was isolated from a subset of the tissue specimens and screened for the presence of K-ras mutations at codon 12.

The normal tissues analyzed were wild-type at codon 12 (GGT = Gly) and codon 13 (GGC = Gly). Of the 13 pancreatic cancer specimens analyzed, one specimen had a mutation at codon 13 whereas 10 samples were mutated at codon 12, corresponding to a K-ras. The extent of COX-2 protein expression. For example, some samples expressed high levels of COX-2 protein and possessed a mutation in K-ras (i.e., tumor samples #9, 16 and 22); however, other samples which had mutated K-ras expressed little or no COX-2 protein (i.e., tumor samples #3, 17, 18, 19, and 21).

with known K-ras mutation status (25, 26). Both the frequency and variability in the quantity of COX-2 expressed in the pancreatic tumor cell lines reflected our findings in the primary pancreatic adenocarcinomas. Of the eight human pancreatic tumor cell lines analyzed, only three of the seven cell lines expressing oncogenic K-ras exhibited detectable levels of COX-2 protein (Capan-1, Capan-2 and Hs578T) (Figure 4B). Taken together, our results suggest that activation of the Ras pathway is not sufficient for mediating COX-2 upregulation in pancreatic tumor cells. We also compared the level of COX-2 expression in three hamster pancreatic cell lines, The D27/K-ras and B 12/13 transformed cell lines and their parental line (Figure 4C). These results confirm our conclusion that Ras activation alone is not sufficient for upregulating COX-2 expression in pancreatic cancer cells and suggest that additional events which occur following exposure to chemical carcinogens may be required.

To examine whether COX-2 expression could be induced in the human

pancreatic cancer cell lines, four cell lines were serum-starved and subsequently treated with 10% FCS for various time periods (Fl crude 4D). In. . . is activated (unpublished observations), again demonstrating that Erk 1/2 activation is not sufficient for inducing COX-2 expression in the COX negative pancreatic tumor cells. We observed similar results upon treating the cell lines with the tumor promoter, PMA (unpublished observations).

Example 3

Treatment of pancreatic tumor cell lines with cyclooxygenase inhibitors

The COX positive human pancreatic tumor cell lines, BxPC-3, and the COX negative cell line, PaCa-2, were treated with the COX inhibitors sulindac, indomethacin, or NS Sulindac and. . . was measured after three days of treatment (Figure 5). All three inhibitors were found to suppress cell growth in both pancreatic tumor cell lines in a dose-dependent manner. However, indomethacin and NS-398 were found to inhibit cell growth to a greater extent in the. . .

To evaluate the functional activity of COX-2 in the human pancreatic tumor cell lines, prostaglandin E2 (PGE₂) production was measured by enzyme immunoassay (Figure 6A). PGE₂ production was elevated in the BxPC-3, Capan-1, Capan-2. . .

These data demonstrate that the combination of sulindac and gemcitabine is more effective than either compound alone in pancreatic tumor cells.

as well as inflammatory agents (5, 6, 29). Recent studies have shown that COX-2 expression is upregulated in a variety of human cancers, including colon, lung, gastric, pancreatic and

esophageal (7-11). In the present study, we report that elevated levels of COX-2 protein are expressed in human pancreatic tumors compared to barely detectable levels in the matched non-tumoral pancreatic tissue, suggesting that increased expression of COX-2 protein correlates with pancreatic tumorigenesis. Our results confirm a recent report demonstrating upregulation of COX-2 RNA and protein in pancreatic tumors and localization of COX-2 in malignant epithelial cells (11). An earlier study demonstrated that the expression of group 11 phospholipase A₂, . . . phospholipids, was higher in pancreatic ductal adenocarcinomas compared to normal pancreatic tissue (30). In addition, the development of N-nitrosobis(2-oxopropyl)amine (BOP)-initiated pancreatic tumors in hamsters was inhibited by the administration of two prostaglandin synthesis inhibitors, phenylbutazone and indomethacin (31). Together with our observations in. . . that increased prostaglandin production due to the increased expression of COX-2 may be an important event in the

multi-step
progression towards pancreatic tumor formation.

as well as prostaglandin E2 were detected in Ras-transformed mammary epithelial cells (C57/MG) cells (17). In human non-small cell lung cancer (NSCLC) cell lines expressing oncogenic K-Ras, increased PGE2 production was mediated by constitutively high expression of cytosolic, phospholipase A, and COX-2 compared. . . . the expression of detectable levels of COX-2 protein. A possible explanation for the lack of COX-2 expression in a subset of the tumors with oncogenic Ras is that Erk1/2 activity may be down-regulated in pancreatic carcinomas (26). Moreover, even in the two pancreatic tumor samples which did show elevated levels of activated Erk1/2 (samples #4 and 21, data not shown), only low levels of COX-2. . . . in the present study, suggesting that Erk1/2 activation alone is not sufficient for inducing COX-2 expression. These findings suggest that within the tumor environment, the presence of oncogenic K-ras does not directly result in increased COX-2 expression in pancreatic cancer.

Similar conclusions were also reached upon analysis of pancreatic cancer cell lines, which were examined since they represent a homogenous population of cells as opposed to primary tumor tissue which is heterogeneous. Despite activating K-ras mutations in seven out of the eight lines, only three of the lines with mutated. . . . of COX-2 expression. Activation of other signaling pathways in addition to Ras may cooperate to determine the extent of COX-2 expression in cancer cells. Such pathways may include the p38 mitogen-activated protein kinase which has been reported to regulate the induction of COX-2 in lipopolysaccharide-treated. . . . the cell type as well as the stimulus. Further experiments will be required to delineate which signaling pathways are function in pancreatic tumor cells.

expressing cell lines. These data suggest that the COX inhibitors exert their inhibitory effects by both COX/PGE₂-dependent and -independent pathways in pancreatic tumor cell lines.

The detection of elevated levels of COX-2 in a variety of human cancers combined with the chemopreventative effect of NSAIDs in colon cancer (10) demonstrate that COX-2 is an important participant in carcinogenesis. The reported biological consequences of COX-2 upregulation include inhibition of apoptosis (13), increased metastatic potential (12) and promotion of

angiogenesis

(14). These events may contribute to cell transformation and tumor progression.

COX-2 expression was noticeably elevated in 55% of the patient pancreatic

tumor samples analyzed, identifying COX-2 as a new target for chemotherapy.

These results demonstrate the ability of COX inhibitors to inhibit pancreatic

tumor cell growth and PGE₂ production in vitro indicate that NSAIDs may be

effective in the treatment of pancreatic cancer patients, for whom few treatment

options currently exist. COX-2 expression is also useful as a prognostic or diagnostic tool.

1. Landis et al., CA Cancer J. Clin., 49, 6-29 (1998).

3. Thun, M.J., Cancer Metastasis Rev., 13, 269-77 (1994).

4. Giardiello et al., Eur. J. Cancer, 31A, 1071-6 (1995).

8. Ristimäki et al., Cancer Res., 57, 1276-80 (1997).

9. Zimmermann et al., Cancer Res., 59, 198-204 (1999).

10. Wolff et al., Cancer Res., 58, 4997-5001 (1998).

11. Tucker et al., Cancer Res., 59, 987-90 (1999).

25. Berrozpe et al., Brit. J. Cancer, 69, 185-91 (1994).

35. Elder et al., Clin. Cancer Res., 3, 1679-83 (1997).

36. Piazza et al., Cancer Res., 57, 2909-15 (1997).

TABLE 1. Analysis of Patient Samples

Tissue Sample Tissue Type % COX-2 b % Cancer K-ras

1 pancreatic adenocarcinoma 7.0 10 WT

2 pancreatic adenocarcinoma 2.0 95

3 pancreatic adenocarcinoma 0.2 15 GGT to CG,

4 pancreatic adenocarcinoma 3.6 . . . N normal 0.1 -

12 pancreatic adenocarcinoma 1 15

14 pancreatic adenocarcinoma 31 ND

Tissue Sample a Tissue Type % COX-2 b % Cancer K-ras

1 5 pancreatic adenocarcinoma 7.8 25 GGT to

15N normal 4.3 - 1

1 6 pancreatic adenocarcinoma 66 35 GGT to

16N non-nal. . . .

c The percent cancer was determined by visualization following hematoxylin/eosin staining of slides prepared from paraffin sections.

CLMEN 1. A method of reducing the viability of pancreatic cancer cells comprising contacting the cancer cells with an effective amount of an NSAID.

2 A method of increasing the susceptibility of mammalian pancreatic cancer cells to a chemotherapeutic agent comprising contacting the cells with an

effective sensitizing amount of an NSAID.

4 The method of claim 1 or 2 wherein the mammalian cancer cells are human cancer cells.

5 The method of claim 3 wherein the sulindac or the analog thereof is administered to a human cancer patient.

6 The method of claim 5 wherein the cancer patient is undergoing treatment with a chemotherapeutic agent.

9 A method of evaluating the ability of sulindac or an analog thereof that is

a COX-2 inhibitor to sensitize pancreatic cancer cells to a chemotherapeutic agent comprising:

(a) isolating a first portion of pancreatic cancer cells from a human

pancreatic cancer patient;

(b) measuring their viability;

(c) administering sulindac or the analog thereof to said patient;

(d) isolating a second portion of pancreatic cancer cells from said

patient;

(e) measuring the viability of the second portion of pancreatic cancer

cells; and

(f) comparing the viability measured in step (e) with the viability measured in step (b); wherein reduced viability in step (e) indicates.

T N T

COX-2 mm 40- cwIIw

C OX- 1

p2i ras

Actin

]1]] VW Iwo ow

C/ (]-)

/8

loo -

90 - lo(

9CF

80-

9

7CF

70-

60-

40

3Y

to 50-

a

cw

C*4 26

40- 1 Cy

0

TUMOR NORMAL

30 -

20-

10-

8

0- 00

TUMOR NORMAL

(n--23)

ylwMian = 5.2% median = 02%
nwan = 15.2 +/- 24.9% mcan 0.83 +/- 1.3%
v2mge = 0 - 93% map 0. . . Sulindac IndometIL NS-398
% inhibition: 0 07 90 F957 98 759 86

/8

Effect of Sulindac + Gemcitabine on the growth of the
pancreatic tumor cell line, BxPC-3 (day 3)

125 -

100 I Gem alone

75 -

1,100+ e

50 - T

em

sul, 500 + Gem

0 5 10 15 20. . . and Technology Institute, Inc.

Marshall, Mark Steven

Sweeney, Christopher J.

Yip-Schneider, Michele T.

Crowell, Pamela L.

10<120> Use of NSAIDs for the treatment of pancreatic cancer

<130> 740.018W01

<150> US 60/165,543

15<151> 1999 15

<160> 2

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 20

<212> DNA

<213> Homo sapiens

<400> 1

atgactgaat ataaacttgt 20

<210> 2

30<211>. . . search (name of data base and, where practical, search
terms used)

EPO-Internal, WPI Data, PAJ,, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS,
CANCERLIT

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category Citation of document, with indication, where appropriate, of
the relevant passages Relevant to claim No.

PqX SWEENEY J. ET AL.: INHIBITION OF CELL 1-11

GROWTH IN PANCREATIC TUMOR CELLS BY

ANTI-INFLAMMATORY DRUGS11

PROCEEDINGS OF THE AMERICAN ASSOCIATION

FOR CANCER RESEARCH,

vol. 41, March 2000 (2000-03),, page 527

XPOO2164391

USA

ABSTRACT #3358

abstract

Further documents are listed in the continuation of box C. Patent family
members. . . passages Relevant to claim NO.

PqX MARSHALL M.S. ET AL.: SUPPRESSION OF 1-11

PANCREATIC DUCTAL ADENOCARCINOMA GROWTH BY

SULINDACH

PROCEEDINGS OF THE AMERICAN ASSOCIATION

FOR CANCER RESEARCH,

vol. 41, March 2000 (2000-03), page 526

XPOO2164392

USA

ABSTRACT #3349

abstract

P9X T.YIP-SCHNEIDER M. ET AL.: COX-2 1-11

EXPRESSION IN HUMAN PANCREATIC

ADENOCARCINOMAS11

CARCINOGENESIS,

vol. 21, no. 2, . . . XPOO0984815
the whole document
X MOLINA M, ET AL.: INCREASED COX-2 1-11
EXPRESSION IN HUMAN PANCREATIC CARCINOMAS
AND CELL LINES: GROWTH INHIBITION NY
NONSTEROIDAL ANTI-INFLAMMATORY DRUGS11
CANCER RESEARCH,
vol. 59, no. 17, September 1999 (1999-09),
pages 4356-4362, XPOO0984712
the whole document
X WO 99 49859 A (THE ARIZONA BOARD OF 1-698
REGENTS).

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	13.17	109.91
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.65

STN INTERNATIONAL LOGOFF AT 09:47:28 ON 14 DEC 2005

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS	1	Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	"Ask CAS" for self-help around the clock
NEWS	3	SEP 09 ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS	4	OCT 03 MATHDI removed from STN
NEWS	5	OCT 04 CA/CAPLUS-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS	6	OCT 13 New CAS Information Use Policies Effective October 17, 2005
NEWS	7	OCT 17 STN(R) AnaVist(TM), Version 1.01, allows the export/download of CAPLUS documents for use in third-party analysis and visualization tools
NEWS	8	OCT 27 Free KWIC format extended in full-text databases
NEWS	9	OCT 27 DIOGENES content streamlined

L4 1026 L2 OR L3

=> s polyanhydride
1149 POLYANHYDRIDE
5384 POLYANHYDRIDES
L5 6164 POLYANHYDRIDE
(POLYANHYDRIDE OR POLYANHYDRIDES)

=> s sulindac
L6 2826 SULINDAC

=> s 16 and 14
L7 16 L6 AND L4

=> s 17 and 15
L8 3 L7 AND L5

=> d ibib 1-3

L8 ANSWER 1 OF 3 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2005081825 PCTFULL ED 20050914 EW 200536
TITLE (ENGLISH): ABUSE RESISTANT OPIOID TRANSDERMAL DELIVERY DEVICE
CONTAINING OPIOID ANTAGONIST MICROSPHERES
TITLE (FRENCH): DISPOSITIF DE DISTRIBUTION TRANSDERMIQUE D'OPIOIDES
EMPECHANT UNE UTILISATION ABUSIVE ET CONTENANT DES
MICROSPHERES D'ANTAGONISTES D'OPIOIDES
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SHAMEEM, Mohammed, 4 Surim Court, Nanuet, NY 10954, US
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10018\$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 2005081825	A2	20050909

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO
CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR
HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV

	MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
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RW (EAPO):	AM AZ BY KG KZ MD RU TJ TM
RW (EPO):	AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT
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RW (OAPI):	BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
APPLICATION INFO.:	WO 2005-US4741 A 20050215
PRIORITY INFO.:	US 2004-60/547,196 20040223

L8 ANSWER 2 OF 3 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 2004052339 PCTFULL ED 20040630 EW 200426
 TITLE (ENGLISH): PH TRIGGERED TARGETED CONTROLLED RELEASE SYSTEMS
 TITLE (FRENCH): SYSTEMES DE LIBERATION CONTROLEE CIBLEE A DECLenchement
 FONCTION DU PH
 INVENTOR(S): SHEFER, Adi, 14 Jason Drive, East Brunswick, NJ 08816,
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 LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE

WO 2004052339	A1	20040624

DESIGNATED STATES
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 RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
 MC NL PT RO SE SI SK TR
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 APPLICATION INFO.: WO 2003-US26142 A 20030821
 PRIORITY INFO.: US 2002-10/315,801 20021209

L8 ANSWER 3 OF 3 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 1996040090 PCTFULL ED 20020514
 TITLE (ENGLISH): METHOD FOR REDUCING OR PREVENTING POST-SURGICAL
 ADHESION FORMATION USING 5-LIPOXYGENASE INHIBITORS
 TITLE (FRENCH): PROCEDE POUR LA REDUCTION OU LA PREVENTION DE LA
 FORMATION D'ADHERENCES POST-CHIRURGICALES A L'AIDE
 D'INHIBITEURS DE 5-LIPOXYDASE
 INVENTOR(S): RODGERS, Kathleen, Elizabeth;
 diZEREGA, Gere, Stodder
 PATENT ASSIGNEE(S): UNIVERSITY OF SOUTHERN CALIFORNIA
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

NUMBER	KIND	DATE

WO 9640090	A1	19961219

DESIGNATED STATES
 W: AU CA JP AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL
 PT SE